

Assessing Alzheimer Severity With a Global Clinical Scale

**J. Wesson Ashford, Vinod Kumar, Mary Barringer,
Marion Becker, Jami Bice, Nelly Ryan, and Sandra Vicari**

ABSTRACT. Diagnosis of dementia needs to be complemented by precise determination of disease severity across the broad spectrum of disease progression. The Mini-Mental State Exam (MMS), the Activities-of-Daily-Living assessment (ADL) and the Clinical Dementia Rating scale (CDR) were modified for direct comparability and administered to 112 outpatients and 45 nursing home residents with a range of dementia severity from mild to profound. The scales showed the highest correlations for the probable Alzheimer's disease patient group (62) (Global Assessment of Dementia; GAD vs. ADL: $r = 0.91$; Extended Mini-Mental Assessment; EMA vs. GAD: $r = 0.91$; ADL vs. EMA: $r = 0.86$). For these patients, scores on the individual scales tended to be similar. Disparity among the three scores for individual cases was associated with the presence of comorbidities. The high correlations and correspondence among these scales demonstrate their reliability, validity, and utility in the assessment of dementia severity. The use of an average of these measures, with their increased precision, may give a more accurate indication of dementia severity over a broader range of impairment.

INTRODUCTION

A basic issue in clinical medicine is the measurement of disease severity. Severity may relate either to stages that distinguish discrete phases of disease progression, or to a continuum that is scaled along a particular dimension. Staging has been applied to dementia (Reisberg et al., 1982; Berger, 1980; Hughes et al., 1982). However, there is no evidence that any one phase of dementia (e.g., mild, moderate, severe, or profound; stage I, II, III, or IV, etc.) constitutes a qualitatively distinct state as compared to any other phase. Rather, many types of dementia are

From the Southern Illinois University School of Medicine, Department of Psychiatry (J. W. Ashford, MD, PhD; V. Kumar, MD; J. Bice, BS [posthumous publication]; S. Vicari, MA, and the Regional Alzheimer Disease Assistance Center (M. Barringer, RNC; N. Ryan, MSW, ACSW), Springfield, IL, USA; and the University of Wisconsin, Madison, WI, USA (M. Becker, MA). New affiliations: University of California, Davis, CA, USA (J. W. Ashford, MD, PhD), and the University of Miami, FL, USA (V. Kumar, MD).

“insidiously progressing” (APA, 1987). The concept of stage conveys a misleading notion of delineation. Instead, the range of dementia needs to be analyzed by more precise and useful scaling approaches.

The need to assess dementia severity has led to the development of numerous scales (Blessed et al., 1968; Folstein et al., 1975; Hughes et al., 1982; Kahn et al., 1960; Lawton, 1983; Mattis, 1976; Meer & Baker, 1965; Rosen et al., 1984). The general validity and utility of these scales has been well established (Applegate et al., 1990). However, the difficult issues in scale design of construct and concurrent validity (Rosen et al., 1986) remain essential considerations. Scale development is difficult in the absence of an established standard, model, or theory. The Blessed scale (Blessed et al., 1968) has been particularly well accepted (Katzman et al., 1989) because of its correlation with an objective measure of Alzheimer pathology, senile plaque counts. However, severity of pathology is difficult to quantitate (Khachaturian, 1985; Ghanbari et al., 1990), and plaque counts may not directly reflect disease severity (Neary et al., 1986) or progression (Mann et al., 1988) or losses of large cortical neurons. Further, there is some degree of heterogeneity in dementia, particularly Alzheimer’s disease (AD), suggesting that dementia severity is affected by multifactorial components (Riege & Metter, 1988; Grady et al., 1990). However, item-by-item evaluation of the variability in AD indicates that there is a strong unidimensional component in the progression of AD (Ashford et al., 1989a) that overshadows the heterogeneity. The dominance of a single factor in explaining dementia severity supports the hypothesis that there is a single, underlying vulnerable brain function—such as neuroplasticity (Ashford & Jarvik, 1985), possibly related to the NMDA-glutamate receptor (Greenamyre et al., 1988)—that is specifically and progressively disrupted in the AD attack (Butcher & Woolf, 1989). A likely direct target of such an attack would be synapses, and loss of synapses from association cortex is a brain measure that also corresponds more closely to dementia severity than plaque counts (Terry et al., 1990). If an underlying homogeneous biological process is at the core of the pathology, then refining measures to assess the state of that process would support the investigation into the cause of the illness. Other scales, such as the Mini-mental State Exam (Folstein et al., 1975), do correlate well with the Blessed scale (Thal et al., 1986) and both scales correspond to measures of synapse loss, pyramidal cell loss, and plaque count (Terry et al., 1991) suggesting that there is some underlying biological validity to the unidimensional approach to scaling dementia severity in AD. However, biological correlates of function are still experimental (Kuhl et al., 1985; Small et al., 1989; Jagust et al., 1990) and quantitative measures of Alzheimer pathology *in vivo* are not currently available, but MRI-T₂ measures are promising (Fazekas et al., 1989; Ashford et al., 1990; Kirsch et al., 1992). Therefore, broad empirical observations of disease progression (Storandt et al., 1986; Wilson & Kaszniak, 1986; Uhlmann et al., 1987; Grady et al., 1988) including psychological, daily function, and global spheres, must be the benchmarks for scale validation.

Both clinicians and researchers need more precise linear assessment tools. However, these tools would be most useful if they corresponded to the approximate terms (i.e., mild, moderate, severe, profound) already used for communicating with patients. We previously demonstrated a high correspondence between the MMS measure and ADL scale measures in patients with primary degenerative dementia ($r = 0.80$; Ashford et al., 1986), supporting the interaction of these measures and their relationship to dementia severity. To improve this approach, we have developed a three-part battery for assessing dementia severity that includes objective and subjective measures, provides precise and reliable assessment over a broader range than other tests, and has considerable clinical validity and utility.

METHOD

Patient Population

Alzheimer Clinic Outpatient Population. The patients in this group (35 males, mean age 72 ± 9 yrs.; 77 females, mean age 75 ± 7 yrs.) had presented to the SIU Alzheimer Clinic for evaluation of memory difficulties. All patients with dementia receiving complete evaluations between July 1986 and June 1989 were included. In every case, the patient was brought in by (usually on the insistence of) a family member or significant other who provided most of the history. All patients received complete evaluations, including physical, neurological, and psychiatric evaluations, neuropsychological testing, EEG or computer brain wave analysis, CT or MRI brain scans, and other appropriate laboratory tests (Wells, 1977). Patients were evaluated for probable, possible, or unlikely AD (McKhann et al., 1984).

Nursing Home Patient Population. The 50 patients in this group (11 males, mean age 76 ± 9 yrs.; 34 females, mean age 83 ± 7 yrs.) were chosen by a random number generated by a computer from 100 patients in a local nursing home as part of the 1986 "Elder Find" project of the Illinois Department of Public Aid; for six cases the data was incomplete. The medical history of each patient was completely reviewed and patients were seen by the project staff on a weekly basis for at least 6 months. The medical status of each patient was thoroughly assessed and progression was monitored over this period. These patients were diverse in their diagnoses, including aphasic stroke patients, severe arthritic patients, and a blind schizophrenic patient.

Evaluation Instruments

Extended Mini-Mental Assessment. The Extended Mini-Mental Assessment (EMA) is a 50-point test of general cognitive status (see Appendix). In the EMA, 30 of the 50 items represented the Mini-Mental State Exam (MMS; Folstein et al., 1975). The MMS is a widely used test because of its value both in documenting the presence of dementia (McKhann et al., 1984) and in assessing its severity and rate of progression (Teng et al., 1987). However, it has two recognized weaknesses: the

first, in distinguishing mild dementia from normal function, and the second, a floor effect (a score of 0) at a middle phase of the illness (Ashford et al., 1989a). In the progression of dementia some skills tend to be lost before others, allowing a short series of questions to give an accurate measure of impairment, following the principles of Likert scaling. Therefore, 20 additional items, frequently cited in the literature for use in assessing dementia progression, were selected to supplement this test. Five supplemental questions were taken from the Mental Status Questionnaire (MSQ; Kahn et al., 1960). Two questions came from the Information, Memory Concentration Test (Blessed et al., 1968; using 16 of 37 items common to these two tests; first and last names separated). Category naming (number of animals in one minute; Battig & Montague, 1969; Cummings & Benson, 1983) was scaled to 5 points. Also included were an abstraction (WAIS; Wechsler, 1958), orientation to time, two items for body orientation (Eslinger et al., 1985), and four measures of appearance and behavior.

Several specific impairments such as mental illness, mental retardation, or visual or hearing impairment can interfere with the administration of cognitive tests. Education also has been suggested to influence performance. Therefore, such tests require judicious use. In assessing a patient with complex problems, individual items rather than the full scale may give a better estimation of specific deficits for determining the need for supportive services and planning assistance. However, in most cases a full range of factors is more useful for estimating the extent of the illness and the overall needs of the patient.

Activities of Daily Living. The Activities-of-Daily-Living scales (ADL) assess instrumental (IADL, Lawton, 1983) and basic (BADL; Linn & Linn, 1983) functions (see Appendix). The IADL scale provides a 23-point range (8–31) while the BADL scale provides a 24-point range (6–30). To bring the total to 50 points in order to balance the tendency of these scales to assess the severe level of function more broadly, a 3-point (0–3) global function question was added that asks the degree of help required by the patient.

The use of ADL for assessing impairment of social function is well established. Though these measures do not provide a true scale, their clinical use in demented patients suggests that there is a progressive loss of functions as dementia becomes more severe. Further, some functions (e.g., shopping ability) clearly tend to be lost before other functions (e.g., grooming). Thus, under uncomplicated circumstances ADL measures provided by a third party give a meaningful index of dementia severity (Loewenstein, et al., 1989).

A variety of conditions especially common in the elderly can interfere with the reliability of the ADL measures for assessing a linear aspect of dementia progression. Arthritis, deformity, other causes of immobility, cardiovascular disease, impairments of vision and hearing, and many other severely disabling illnesses that affect the body but spare the mind can impair ADL function. Third-party observers are usually reliable, but they may give distorted views of function. Environmental factors may make coping unusually difficult or easy. Atypical

settings, including rural locales and nursing facilities, can provide especially strong support mechanisms or can insulate a patient from the usual challenges of life and decrease the validity of the assessed ADL performance level. Sometimes a spouse or significant other may misreport the patient's actual capacities. Such misreports could be due to a variety of factors such as poor observation, attempting to cover for a spouse's deficits, or idiosyncratic adaptations. Therefore, the ADL measure must be used carefully when applied to the measurement of dementia. This potential unreliability highlights the importance of comparing this assessment with other measures when determining the patient's need for care.

Global Assessment of Dementia. The Global Assessment of Dementia (GAD) provides a 50-point assessment of impairment in 3 realms (see Appendix) with a total of 10 measures of memory (3 items), higher cognitive function (4 items), and social function (3 items) corresponding to DSM-III-R dementia criteria A, B, and C (APA, 1987). Each of the 10 items of this scale is a 6-point (0-5) assessment of severity in that dimension. Anchor points for levels 0, 1, 2, and 3 are based on the Clinical Dementia Rating scale (CDR; Berg et al., 1982) for 7 of the items, with additional items and anchor points derived from the Haycox Scale (Haycox, 1984), the Global Deterioration Scale (GDS; Reisberg et al., 1982), and the personality inventory of the Blessed dementia scale (Blessed et al., 1968). Memory is given additional bias by having a recent and remote category as in the CDR (Hughes et al., 1982). General homogeneity or heterogeneity of the dementia symptoms can be assessed by dividing the score by 10 and comparing the result to each of the 10 individual items, indicating the relative strengths and weaknesses of the patient. The GAD scale provides a broad assessment of those functions most commonly affected by dementia. The scale includes an inventory of criteria for a DSM-III-R diagnosis of dementia. The CDR scale is one of the most widely used scales for globally assessing dementia. However, this scale uses a complicated scoring system that eliminates precision and is inadequate for assessing patients beyond the midstage of the illness. (Note: The mild, moderate, and severe anchor points of the GAD are consistent with those levels described in the CDR, but our scale added the "profound" category to adequately evaluate nursing home patients.) The Haycox Scale was developed for nursing home patients (it is inadequate for assessing mild and moderate patients), and was considered in developing the severe and profound categories.

Personality changes, while difficult to quantitate, are present even early in AD (Rubin & Kinscherf, 1989). Since personality change is considered to be an important aspect of dementia (it is a criterion item of DSM-III-R), a personality component was included in the GAD. However, the Blessed scale, from which the personality items were derived, has the only demonstrated association with the severity of senile plaque pathology in the brain. Therefore, items from the Blessed scale were used in creating the GAD personality subscale.

50-Point Scaling System. Each part of the assessment (EMA, ADL, and GAD, independently) yields a computed score between 0 and 50 points. Anchor points and

item credits were subjectively selected or adjusted in the early phase of instrument development to provide results that could be consistent with the following scheme:

- 0–2 No significant deficits
- 3–5 Questionable dementia
- 6–15 Mild impairment
- 16–25 Moderate impairment
- 26–35 Severe impairment
- 36–45 Profound impairment
- 46–50 Complete impairment

This system introduces no new items for assessing dementia. Each of the items is derived from other tests that have been examined and shown to have high test-retest reliability (e.g., Folstein, Haycox) or objective validity (Blessed et al., 1968). Because the three scales have been adjusted to the same anchor points, scores on different scales can be directly compared. For clinical purposes, in appropriate conditions the three scores can be averaged to give a composite score that follows the same scheme and offers a useful single measure of dementia severity.

System Administration. In the outpatient clinic the ADL scales were administered by a nurse, and the EMA (including the MMS) and the GAD were administered by a psychiatrist. In the nursing home, the ADL and EMA scales were administered by a project nurse or researcher, and the GAD scale was completed during discussion with a psychiatrist.

Data Analysis

The test scores for both groups were analyzed for mean and standard deviation. In addition, regression analyses were performed to determine correlations between test scores. The Pearson product-moment correlation coefficient (r) was determined to give an index of the predictability of one individual's score given another related score. A second indicator determined by these analyses was the slope of the regression line. The slope characterized the mathematical rate of change across dementia severity for each measure. The y-intercept of the regression line also was calculated and indicated the degree of scale correspondence.

RESULTS

Correlations were analyzed among the MMS, EMA, IADL, BADL, ADL, and GAD across all of the patients (Table 1). For the 112 outpatients in the sample, there was a modest correlation among the scales (Table 2). For the 45 nursing home patients, the correlation was less robust (Table 3). However, for the 62 probable Alzheimer patients from both groups, there was a closer relationship (Table 4, Figures 1, 2).

The mean scores for the three scales were similar in the outpatients (EMA = 17; ADL = 16; GAD = 14). For the nursing home patients whose scores were much

TABLE 1. All Patients: Correlations among 50-point Scales and the Parent Scales. All Correlations Significant at $p < 0.001$.

	EMA	IADL	BADL	ADL	GAD
MMS	-0.97	-0.87	-0.64	-0.70	-0.87
EMA		0.71	0.68	0.74	0.88
IADL			0.78	0.96	0.74
BADL				0.92	0.79
ADL					0.81

TABLE 2. All Outpatients: Top: Same as Table 1. Bottom: Slopes and Intercepts of Regression line for the 50-point scales.

	EMA	IADL	BADL	ADL	GAD
MMS	-0.97	-0.75	-0.66	-0.77	-0.89
EMA		0.77	0.70	0.80	0.91
IADL			0.78	0.96	0.82
BADL				0.90	0.78
ADL					0.90

	Slope	Intercept
EMA vs. GAD	1.44	0.8
EMA vs. ADL	2.19	0.8
ADL vs. GAD	1.06	1.0

TABLE 3. All Nursing Home Patients: Same as Table 2.

	EMA	IADL	BADL	ADL	GAD
MMS	-0.98	-0.48	-0.55	-0.57	-0.83
EMA		0.51	0.58	0.60	0.83
IADL			0.65	0.86	0.59
BADL				0.95	0.73
ADL					0.74

	Slope	Intercept
EMA vs. GAD	0.84	0.6
EMA vs. ADL	0.42	23.8
ADL vs. GAD	0.49	23.7

TABLE 4. All Probable AD: Same as Table 2.

	EMA	IADL	BADL	ADL	GAD
MMS	-0.97	-0.79	-0.76	-0.84	-0.88
EMA		0.82	0.79	0.86	0.91
IADL			0.79	0.96	0.84
BADL				0.91	0.89
ADL					0.91
			Slope	Intercept	
EMA vs. GAD			1.01	3.3	
EMA vs. ADL			0.91	0.8	
ADL vs. GAD			1.04	1.4	

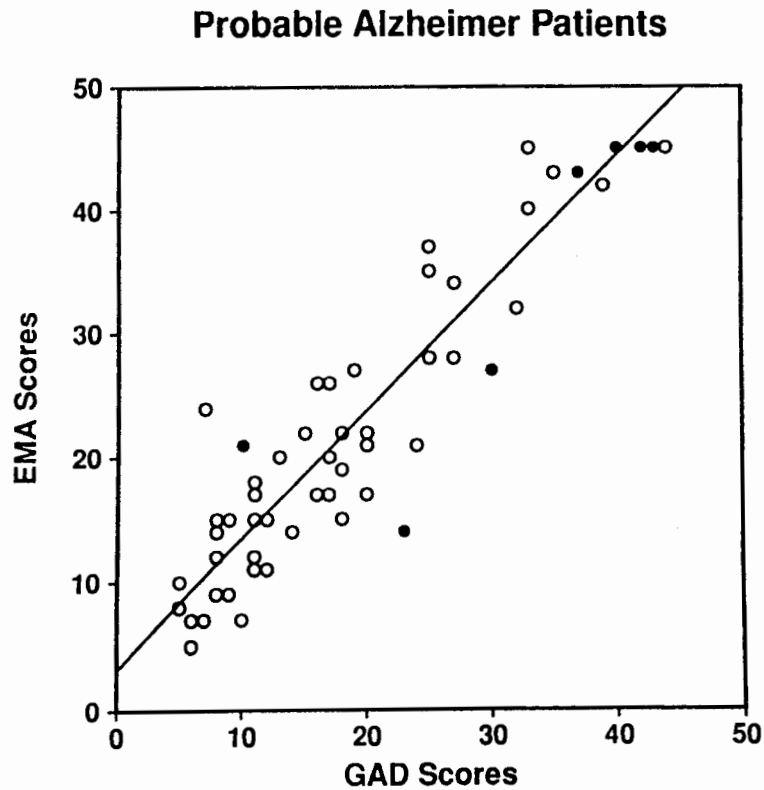


Figure 1. Comparison of GAD and EMA scores for probable Alzheimer patients. Open circles: outpatients; solid circles: nursing home patients.

lower overall, the mean ADL score was much higher compared to the other two test scores (EMA = 27; ADL = 35; GAD = 23). The variation among scale scores presumably depended on several factors. ADL scores would be expected to be relatively higher for a nursing home population, since functional impairment may predispose to placement, and instrumental skill maintenance is usually not fostered in this setting. Also, many of the patients, particularly in the nursing home, had specific physical problems that impaired daily function but not mental state. Improvement in the correlations might be achieved by accounting for these issues as well as factors such as age and prior intellectual function.

A close correspondence among scales for individual patients indicates a high reliability for these severity measures. The correspondence could be estimated from the standard deviation (STD) of the values for EMA, ADL, and GAD. When the STD was less than 5, the three scores tended to be within 10 points. The STD

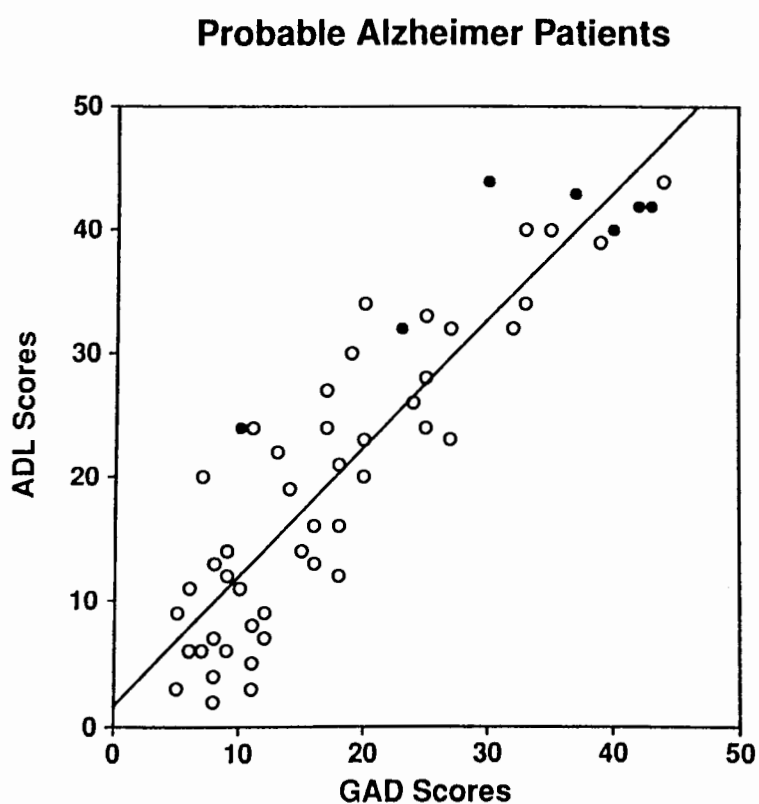


Figure 2. Comparison of GAD and ADL scores for probable Alzheimer patients. Open circles: outpatients; solid circles: nursing home patients.

was less than 5 for 51/55 (93%) of the probable Alzheimer outpatients and all of the probable Alzheimer nursing home patients. Only 12/38 (32%) of the other nursing home patients showed such a relationship, mostly because the ADL score tended to be relatively poor in the nursing home setting. The slopes were closest to 1 for the probable Alzheimer group and the intercepts closest to the origin. Thus, the scores were most reliable for the probable Alzheimer outpatients; therefore, the average score would have the most clinical utility for this population.

When compared with their parent scales, the EMA and ADL showed consistently better correlations. However, the general correspondence among the scales was consistent.

DISCUSSION

This study indicates that cognitive mental status, activities-of-daily-living functions, and global dementia state can be used to measure dementia severity with more precision than is possible with the most widely used scales. These measures have been adjusted so that the degree of severity in each domain is easily compared. The correlation among these measures is strongest in cases of probable AD that are not complicated by physical disease. The high correlations among the measures in this study are likely to be due at least in part to the broad range and high precision of each test. Use of the composite of these of these three measures with their increased precision is likely to give more accurate, more reliable, and more valid indications of dementia severity over a broader range of impairment than individual tests.

Precise measures of dementia severity are useful for clinical assessment. In an individual patient, lack of correspondence among the scales may indicate that noncognitive factors have not been adequately evaluated or are impairing the patient's function. Such information will better delineate the patient's needs and allow for more responsive coordination of services. In carefully selected patients, these scales correlate highly with another functionally relevant objective measure, choice reaction time (Ashford et al., 1989b). Though such high correlations had not been obtained between functional measures and any biological index, a recent study did show a close relationship between function and loss of synapses in frontal and temporal cortex (Terry et al., 1991). The high correlation among independently acquired data suggests that some physical factor must underlie the severity dimension. Ultimately, the most important consideration is establishing methods for accurately determining the relationship between function and the underlying neuropathology. Increased precision of dementia assessment will support research into disease progression, environmental factors associated with the progression, and the efficacy of therapeutic interventions.

There are several clinical approaches suggested by the correspondence among these scales. A global assessment by a physician reliably indicates the approximate level of dementia assessed by an objective test and estimates the functional capacity

of the patient in the environment. The objective test confirms the global assessment and also predicts the current level of functional incapacity. Measures of daily living function reflect objective dysfunction and correspond well to neuropathology (Blessed et al., 1968; Terry et al., 1991) though autopsy studies reflect only the status at the terminal phase of the illness, which is likely to be severe (Kaszniak et al., 1978). Thus, any one of these tests could be used alone, efficiently and effectively, as a screening tool in clinical or epidemiological research settings, when precision of severity assessment is less critical.

An additional important problem in studying dementia is determining the rate of progression of the disease. Single-point measures in a variety of patients can estimate only the general pattern of disease progression. Actual progression and rates of deterioration require longitudinal assessments. Measuring the 50-point composite score at intervals in the same patient would add considerable depth to understanding dementia progression. Also, individual items on these tests can be examined using item characteristic curve analysis techniques (Ashford et al., 1989a) to further specify which items assess severity on the linear dimension most usefully. The 50-point system could be useful in assessing community-dwelling dementia patients, especially if rate of deterioration would predict the need for utilization of various respite care services that could be available in the community, or the need for nursing home placement.

REFERENCES

- American Psychiatric Association Task Force on Nomenclature and Statistics. (1987). *Diagnostic and statistical manual of mental disorders* (3rd ed., rev.). Washington, DC: American Psychiatric Association.
- Applegate, W. B., Blass, J. P., & Williams, T. F. (1990). Instruments for the functional assessment of older patients. *England Journal of Medicine*, *17*, 1207–1214.
- Ashford, J. W., & Jarvik, L. F. (1985). Alzheimer's disease: Does neuronal plasticity predispose to axonal neurofibrillary degeneration? *New England Journal of Medicine*, *313*, 388–389.
- Ashford, J. W., Hsu, L. N., Becker, M., Kumar, V., & Bekian, C. (1986). Minimental status and activities of daily living: Cross validation by scalogram and item analysis techniques. *The Gerontologist*, *26*, 143A.
- Ashford, J. W., Kolm, P., Colliver, J. A., Bekian, C., & Hsu, L. N. (1989a). Alzheimer patient evaluation and the mini-mental state: Item characteristic curve analysis. *Journals of Gerontology: Psychological Sciences*, *44*(5), P139–P146.
- Ashford, J. W., Bice, J., Vicari, S., & Feldman, E. (1989b). Simple choice reaction vs. Alzheimer severity. *The Gerontologist*, *29*, 140A.
- Ashford, J. W., Rashid, A., Lawrance, D., Calache, M., Bice, J., et al. (1990). AD pathology: In vivo quantitation by MRI? *Society of Neuroscience Abstract*, *389*, 3.
- Battig, W. F., & Montague, W. E. (1969). Category norms for verbal items in 56 categories: A replication and extension of the Connecticut category norms. *Journal of Experimental Psychology Monograph*, *80*, 1–43.

- Berg, L., Hughes, C. P., Coben, L. A., Danziger, W. L., Martin, R. L., et al. (1982). Mild senile dementia of the Alzheimer type (SDAT): Research diagnostic criteria, recruitment, and description of a study population. *Journal of Neurology, Neurosurgery, & Psychiatry*, *45*, 962–968.
- Berger, E. Y. (1980). A system for rating the severity of senility. *Journal of the American Geriatrics Society*, *23*, 234–236.
- Blessed, G., Tomlinson, B. E., & Roth, M. (1968). The association between quantitative measures of dementia and of senile change in the cerebral grey matter in elderly subjects. *British Journal of Psychiatry*, *114*, 797–811.
- Butcher, L. C., & Woolf, N. J. (1989). Neurotrophic agents may exacerbate the pathological cascade of Alzheimer's disease. *Neurobiology of Aging*, *10*, 557–570.
- Cummings, J. L., & Benson, D. F. (1983). *Dementia: A clinical approach*. Stoneham, MA: Butterworth Publishers.
- Eslinger, J., Damasio, A. R., Benton, A. L., & Van Allen, M. (1985). Neuropsychological detection of abnormal mental decline in older persons. *Journal of the American Medical Association*, *253*, 670–674.
- Fazekas, F., Alavi, A., Chawluk, J. B., Zimmerman, R. A., Hackney, D., et al. (1989). Comparison of CT, MR, and PET in Alzheimer's dementia and normal aging. *Journal of Nuclear Medicine*, *30*(10), 1607–15.
- Folstein, M. J., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state:" A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, *12*, 189–198.
- Ghanbari, H. A., Miller, B. E., Haigler, H. J., Arato, M., Bissette, G., et al. (1990). Biochemical assay of Alzheimer's-disease-associated protein(s) in human brain tissue: A clinical study. *Journal of the American Medical Association*, *263*, 2907–2910.
- Grady, C. L., Haxby, J. V., Horwitz, B., Sundaram, M., Berg, G., et al. (1988). Longitudinal study of the early neuropsychological and cerebral metabolic changes in dementia of the Alzheimer type. *Journal of Clinical and Experimental Neuropsychology*, *10*, 576–596.
- Grady, C. L., Haxby, J. V., Schapiro, M. B., Gonzalez-Aviles, A., Kumar, A., et al. (1990). Subgroups in dementia of the Alzheimer type identified using positron emission tomography. *Journal of Neuropsychiatry*, *2*, 373–384.
- Greenamyre, J. T., Maragos, W. F., Albin, R. L., Penney, J. B., & Young, A. B. (1988). Glutamate transmission and toxicity in Alzheimer's disease. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *12*, 421–430.
- Haycox, J. A. (1984). A simple, reliable clinical behavioral scale for assessing demented patients. *Journal of Clinical Psychiatry*, *45*, 23–24.
- Hughes, C. P., Berg, L., Danziger, W. L., Coben, L. A., & Martin, R. L. (1982). A new clinical scale for the staging of dementia. *British Journal of Psychiatry*, *140*, 566–572.
- Jagust, W. J., Reed, B. R., Seab, J. P., & Budinger, T. F. (1990). Alzheimer's disease: Age at onset and single-photon emission computed tomographic patterns of regional cerebral blood flow. *Archives of Neurology*, *47*, 628–633.
- Kahn, R. L., Goldfarb, A. I., & Pollack, M. (1960). Brief objective measures for the determination of mental status in the aged. *American Journal of Psychiatry*, *117*, 326–328.
- Kasznik, A. W., Fox, J., Gandell, D. L., Garron, D. C., Huckman, M. S., & Ramsey, R. G. (1978). Predictors of mortality in presenile and senile dementia. *Annals of Neurology*, *3*, 246–252.

- Katzman, R., Aronson, M., Fuld, P., Kawas, C., & Brown, T. (1989). Development of dementing illnesses in an 80-year-old volunteer cohort. *Annals of Neurology*, *25*, 317–324.
- Khachaturian, Z. S. (1985). Diagnosis of Alzheimer's disease. *Archives of Neurology*, *42*, 1097–1104.
- Kirsch, S. J., Jacobs, R. W., Butcher, L. L., & Beatty, J. (1992). Prolongation of magnetic resonance T₂ time in hippocampus of human patients marks the presence and severity of Alzheimer's disease. *Neuroscience Letters*, *134*, 187–190.
- Lawton, M. P. (1983). Assessment of behaviors required to maintain residence in the community. In T. Crook, S. Ferris, & R. Bartus (Eds.), *Assessment in geriatric psychopharmacology*. New Canaan, CT: Mark Powley Associates, Inc.
- Linn, M. W., & Linn, B. S. (1983). Assessing activities of daily living in institutional settings. In T. Crook, S. Ferris, & R. Bartus (Eds.), *Assessment in geriatric psychopharmacology*. New Canaan, CT: Mark Powley Associates, Inc.
- Loewenstein, D. A., Amigo, E., Duara, R., Guterman, A., Hurwitz, D., et al. (1989). A new scale for the assessment of functional status in Alzheimer's disease and related disorders. *Journal of Gerontology*, *44*, 114–121.
- Mann, D. M. A., Marcyniuk, B., Yates, P. O., Neary, D., & Snowden, J. S. (1988). The progression of the pathological changes of Alzheimer's disease in frontal and temporal neocortex examined both at biopsy and at autopsy. *Neuropathology and Applied Neurobiology*, *14*, 177–195.
- Mattis, S. (1976). Mental status examination for organic mental syndrome in the elderly patient. In L. Bellak & T. B. Karasu (Eds.) *Geriatric psychiatry*. New York: Grune & Stratton.
- McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. (1984). Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA work group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology*, *34*, 939–944.
- Meer, B., & Baker, I. A. (1965). The Stockton geriatric rating scale. *Journal of Gerontology*, *20*, 392–403.
- Neary, D., Snowden, J. S., Mann, D. M. A., Bowen, D. M., Sims, N. R., et al. (1986). Alzheimer's disease: a correlative study. *Journal of Neurology, Neurosurgery, and Psychiatry*, *49*, 229–237.
- Reisberg, B., Ferris, S. H., & de Leon, M. J. (1982) The global deterioration scale for assessment of primary degenerative dementia. *American Journal of Psychiatry*, *139*, 1136–1139.
- Riege, W. H., & Metter, E. J. (1988). Cognitive and brain imaging measures of Alzheimer's disease. *Neurobiology of Aging*, *9*, 69–86.
- Rosen, V. L. G., Mohs, R. C., & Davis, K. L. (1984). A new rating scale for Alzheimer's disease. *American Journal of Psychiatry* *141*(11), 1356–1364.
- Rosen, W. G., Mohs, R. C., & Davis, K. L. (1986). Longitudinal changes: Cognitive, behavioral, and affective patterns in Alzheimer's disease. In L. W. Poon (Ed.), *Handbook for clinical memory assessment of older adults*. Washington, DC: American Psychological Association.
- Rubin, E. H., & Kinschurf, D. A. (1989). Psychopathology of very mild dementia of the Alzheimer type. *American Journal of Psychiatry*, *146*, 1017–1021.
- Small, G. W., Kuhl, D. E., Riege, W. H., Fujikawa, D. G., Ashford, J. W., et al. (1989). Cerebral glucose metabolic patterns in Alzheimer's disease: Effect of gender and age at dementia onset. *Archives of General Psychiatry*, *46*, 527–532.

- Storandt, M., Botwinick, J., & Danziger, W. L. (1986). Longitudinal changes: Patients with mild SDAT and matched healthy controls. In L. W. Poon (Ed.), *Handbook for clinical memory assessment of older adults*. Washington, DC: American Psychological Association.
- Teng, E. L., Chui, H. C., Schneider, L. S., & Metzger, L. E. (1987). Alzheimer's dementia: Performance on the mini-mental state examination. *Journal of Consulting and Clinical Psychology, 55*, 96-100.
- Terry, R., Masliah, E., Salmon, D., Butters, N., DeTeresa, R. et al. (1991). Physical basis of cognitive alterations in Alzheimer's disease: Synapse loss is the major correlation of cognitive impairment. *Annals of Neurology, 30*, 572-580.
- Thal, L. J., Grundman, M., & Golden, R. (1986). Alzheimer's disease: A correlational analysis of the Blessed Information-Memory-Concentration test and the Mini-mental state exam. *Neurology, 36*, 262-264.
- Uhlmann, R. F., Larson, E. B., & Buchner, D. M. (1987) Correlations of minimal state and modified dementia rating scale to measures of transitional health status in dementia. *Journal of Gerontology, 42*(1), 33-36.
- Wechsler, D. (1958). *The measurement and appraisal of adult intelligence*. Baltimore, MD: Williams and Wilkins.
- Wells, C. E. (1977). *Dementia*. Philadelphia: F. A. Davis Company.
- Wilson, R. S., & Kaszniak, A. W. (1986). Longitudinal changes: Progressive idiopathic dementia. In L. W. Poon (Ed.), *Handbook for clinical memory assessment of older adults*. Washington, DC: American Psychological Association.

Offprints. Requests for offprints should be sent to J. Wesson Ashford, MD, PhD, Veterans Affairs Clinic-116A, Department of Psychiatry, University of California - Davis, 150 Muir Road, Martinez, CA, 94553 U.S.A.

APPENDIX

Instrumental Activities of Daily Living Scale (Adapted from Lawton, 1983)

-
1. Ability to use telephone _____
 - 0 = Operates telephone on own initiative—looks up and dials numbers, etc.
 - 1 = Dials a few well-known numbers
 - 2 = Answers telephone but does not dial
 - 3 = Does not use telephone at all (could if necessary)
 - 4 = Incapable of using telephone
 2. Shopping _____
 - 0 = Takes care of all shopping needs independently
 - 1 = Shops independently for small purchases
 - 2 = Needs to be accompanied on any shopping trip
 - 3 = Completely unable to shop
 3. Food preparation..... _____
(If never prepared meals, note and score according to related abilities)
 - 0 = Plans, prepares, and serves adequate meals independently
 - 1 = Prepares adequate meals if supplied with ingredients
 - 2 = Heats and serves prepared meals, or prepares meals
 - 3 = Needs to have meals prepared and served

- 4. Housekeeping _____
 (If never did housekeeping, note and score according to related abilities)
 0 = Maintains house alone or with occasional assistance (e.g., "heavy work-domestic help")
 1 = Performs light daily tasks such as dish washing, bed making
 2 = Performs light daily tasks but cannot maintain acceptable level of cleanliness
 3 = Needs help with all home maintenance tasks
 4 = Is unable to participate in any housekeeping tasks
- 5. Laundry..... _____
 (If never did laundry, note and score according to related abilities)
 0 = Does personal laundry completely
 1 = Launders small items, rinses socks, stockings, etc.
 2 = All laundry must be done by others
- 6. Mode of transportation _____
 0 = Travels independently on public transportation or drives own car
 1 = Arranges own travel via taxi, but does not otherwise use public transportation
 2 = Travels on public transportation when assisted or accompanied by another
 3 = Travel limited to taxi or automobile with assistance of another
- 7. Responsibility for own medication _____
 0 = Is responsible for taking medication in dosages at correct time
 1 = Takes responsibility if medication is prepared in advance in separate dosages
 2 = Is not capable of dispensing own medication
- 8. Ability to handle finances _____
 0 = Manages financial matters independently (budgets, writes checks, pays rent and bills, goes to bank), collects and keeps track of income
 1 = Manages day-to-day purchases, but needs help with banking, major purchases, etc.
 2 = Incapable of handling money
- Total Score (Max = 23)..... _____

Physical Self-Maintenance Scale
 (Adapted from Linn & Linn, 1983)

- 9. Toilet..... _____
 0 = Cares for self at toilet completely, no incontinence
 1 = Needs to be reminded, or needs help in cleaning self, or has rare (weekly at most) accidents
 2 = Soiling or wetting while asleep more than once a week
 3 = Soiling or wetting while awake more than once a week
 4 = No control of bowels or bladder
- 10. Feeding _____
 0 = Eats without assistance
 1 = Eats with minor assistance at meal times, with help in preparing food or with help in cleaning up after meals
 2 = Feeds self with moderate assistance and is untidy
 3 = Requires extensive assistance for all meals
 4 = Does not feed self at all and resists efforts of others to feed him/her
- 11. Dressing _____
 0 = Dresses, undresses, and selects clothes from own wardrobe
 1 = Dresses and undresses self, with minor assistance
 2 = Needs moderate assistance in dressing or selection of clothes
 3 = Needs major assistance in dressing, but cooperates with efforts of others to help
 4 = Completely unable to dress self and resists efforts of others to help

- 12. Grooming (neatness, hair, nails, hands, face, clothing) _____
 - 0 = Always neatly dressed, well-groomed, without assistance
 - 1 = Grooms self adequately with occasional minor assistance, e.g., in shaving
 - 2 = Needs moderate and regular assistance or supervision in grooming
 - 3 = Needs total grooming care, but can remain well-groomed after help from others
 - 4 = Actively negates all efforts of others to maintain grooming
- 13. Physical Ambulation _____
 - 0 = Goes about grounds or city
 - 1 = Ambulates within residence or about one-block distance
 - 2 = Ambulates with assistance of another person, railing, cane, walker, or wheelchair
 - 3 = Sits unsupported in chair or wheelchair, but cannot propel self without help
 - 4 = Bedridden more than half the time
- 14. Bathing _____
 - 0 = Bathes self (tub, shower, sponge bath) without help
 - 1 = Bathes self with help in getting in and out of tub
 - 2 = Washes face and hands only, but cannot bathe rest of body
 - 3 = Does not wash self, but is cooperative with those who bathe him or her
 - 4 = Does not try to wash self and resists efforts to keep him or her clean
- Total Score (Max = 24) _____
- 15. Global Function _____
 - 0 = Able to live independently without assistance
 - 1 = Because of memory problems, requires at least weekly visit by outside support person, or mildly reliant on companion
 - 2 = Requires daily help to function
 - 3 = Requires help in all areas of function during day; cannot be left alone or requires medication for behavioral control
- Total ADL Score (Max = 50) _____

Extended Mini-Mental Assessment (EMA)—Extension

Questions	Patient Responses	Score
What is your full name?	First _____ (1) Last _____ (1)	_____
How old are you?	Age _____ (1)	_____
When is your birthday?	Date _____ (1)	_____
When were you born?	Year _____ (1)	_____
Who is the U.S. President?	Pres. _____ (1)	_____
Who was President before him?	Past _____ (1)	_____
How are an orange and a banana alike?	Fruit _____ (1)	_____
Name as many animals as you can in one minute. (If the patient has difficulties getting started, suggest that he or she think of the zoo, the farm, or the jungle.)	Number _____ (1) _____ _____ _____ _____ _____ _____ _____ _____ _____	_____
1 = 1 point		
2-5 = 2 points		
6-10 = 3 points		
11-15 = 4 points		
>15 = 5 points		

Show me your right hand. Single _____ (1) _____
 Touch your right ear with your left hand. Double _____ (1) _____
 What is the exact time of day? Time _____ (1) _____
 (within 1 hour; caution patient not to look at a clock)

Abilities:

Utters coherent words. Words _____ (1) _____
 Speaks complete sentences. Sentences _____ (1) _____
 Sits unassisted. Sits _____ (1) _____
 Exhibits voluntary movements. Moves _____ (1) _____
 Extension Score _____ (20)

Mini-Mental State Exam
 (Folstein, Folstein, & McHugh, 1975)

I. Orientation (Ask the following questions)

What is today's date? Date _____
 What is the year? Year _____
 What is the month? Month _____
 What day is today? Day _____
 What season is it? Season _____
 What is the name of this place? (accept clinic etc.) Place _____
 What floor are we on? Floor _____
 What town or city are we in? Town _____
 What county are we in? County _____
 What state are we in? State _____

II. Immediate Recall

Ask the subject if you may test his/her memory. "Ball" _____
 Then say "ball," "flag," "tree" clearly and slowly, "Flag" _____
 about 1 second for each. After you have said all 3 "Tree" _____
 words, ask him/her to repeat them. The first repetition determines the score (0-3), but keep saying them until he/she can repeat all 3, up to 6 tries. If he/she does not eventually learn all 3, recall cannot be meaningfully tested.
 Note # trials _____

III. Attention and Calculation

A) Ask the subject to begin with "93" _____
 100 and to count backward "86" _____
 by 7. Stop after 5 sub- "79" _____
 tractions. Score the total "72" _____
 number of correct answers. "65" _____
 total _____

B) Ask the subject to spell the "D" _____
 word "world" backward. The "L" _____
 score is the number of letters "R" _____
 in correct position. For ex- "O" _____
 ample, "dlrow" is 5, "dlorw" "W" _____
 is 3, "lrowd" is 0. total _____

Highest score of A or B _____

IV. Recall		
Ask the subject to recall the 3 words you previously asked him/her to remember.	"Ball"	_____
	"Flag"	_____
	"Tree"	_____
V. Language		
Naming: Show the subject a wristwatch and ask him/her what it is. Repeat for pencil.	Watch	_____
	Pencil	_____
Repetition: Ask subject to repeat: "No ifs, ands, or buts."	Repetition	_____
Reading: Show the subject a card that reads, "Close your eyes." Ask him/her to read it and to do what it says. Score only if the subject closes his/her eyes.	Closes eyes	_____
3-Stage Command: Give the subject a plain piece of paper and say, "Take the paper in your hand, fold it in half, and put it on the floor."	Paper in hand	_____
	Folds in half	_____
	Puts on floor	_____
Writing: Ask him/her to write a sentence on the paper. It must contain a subject and a verb and be sensible. Correct grammar and punctuation are not necessary.	Writes sentence	_____
Copying: On the paper, ask the subject to draw intersecting pentagons (give example), each about 1 inch on a side. All 10 angles must be present and 2 must intersect to score 1 point (ignore tremor and rotation).	Draws pentagons	_____
Deriving Total Score: Sum the number of correct replies to the test items. The maximum score is 30 for this test.	MMS Score (30)	_____
(EMA Score = 50—Extension Total—MMS Total)	EMA Score (50)	_____

DSM-III-R Inventory and Global Assessment of Dementia Stage (GAD)

A) Demonstrable evidence of impairment of short- and long-term memory

A1) Recent memory, attention

0 = Memory for daily events unquestioned.

1 = Occasional failures to recall recent events, placement of objects such as keys. Defect interferes with everyday activities.

2 = New material rapidly lost, easily distracted.

3 = Wandering attention.

4 = Can be engaged only sporadically and briefly.

5 = No attention to environmental events.

A2) Remote memory, awareness

- 0 = Clarity with considerable details in recollection of events from childhood and early adulthood.
- 1 = Memory for significant events of the past, but some uncertainty and lack of details.
- 2 = Clear deficits in memory of personal history, some difficulty recalling names of familiar friends, relatives. Recalls place of birth, name of school, occupation, major past events.
- 3 = Unable to recall any historical events or places of schooling. May occasionally forget name of spouse or most frequent caregiver.
- 4 = Difficulties with awareness of environment, sometimes able to distinguish familiar persons from unfamiliar persons, knows own name.
- 5 = No awareness of the nature of the surroundings.

A3) Orientation

- 0 = Fully oriented.
- 1 = Some difficulty with time relationships, date not known, difficulty with year. May have problems with getting lost.
- 2 = Usually disoriented in time, often disoriented to place.
- 3 = Orientation to person only.
- 4 = Body disorientation.
- 5 = Totally lost, oblivious to posture.

B) Impairment of cognition—higher cortical function

B1,2) Judgment, problem solving, abstract thinking

- 0 = Solves everyday problems well; judgment good in relation to past performance.
- 1 = Mild difficulty in handling complex problems, similarities, differences; social judgment usually maintained.
- 2 = Moderately impaired in handling problems; social judgment usually impaired.
- 3 = Unable to make judgments or to solve problems.
- 4 = Unable to carry a thought long enough to determine a purposeful course of action.
- 5 = No response to any confronted problem.

B3a) Language function, aphasia (dominant hemisphere)

- 0 = Conversational, no searching for words.
- 1 = Reticent conversation, searches for synonyms, word or name finding difficulties evident to intimates.
- 2 = Vocabulary limitations noted in conversation, difficulty in naming objects.
- 3 = Conversation limited to use of simple words and sentences. Can name simple objects but not uncommon objects.
- 4 = Speech limited to single simple words, difficulty repeating single words, incomprehending.
- 5 = All verbal abilities lost, mute, unresponsive.

B3b) Visuospatial organization, agnosia (nondominant hemisphere)

- 0 = No difficulty with three-dimensional perspectives; identifies the purpose of complex objects and can use them.
- 1 = Mild difficulty copying complex three-dimensional designs, has difficulty recalling the purpose of unusual objects.
- 2 = Considerable difficulty in reproducing simple drawings, can use simple objects only.
- 3 = Unable to use writing implement for copying a simple design, misidentifies objects.
- 4 = Can respond meaningfully only to some very familiar objects, e.g., may hold brush by handle, take pencil in hand, cannot fully use these objects.
- 5 = Unresponsive to objects in the environment.

B4) Personality changes and emotional responsiveness

- 0 = No acquaintance of the patient has noticed any change in personality.
- 1 = Close acquaintances of patient have noticed some alterations of personality or accentuation of premorbid traits.
- +1 = Increased rigidity or less responsive to environment.
- +1 = Increased egocentricity or life internalized.
- +i = Impairment of regard for feelings of others or decrease of awareness of the way others feel.
- +1 = Impairment of emotional responsiveness, either by lack of control or blunting of affect.

C) The disturbance of memory (A) and cognition (B) significantly interferes with work or usual social activities or relationships with others:

